DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Compound H and troglitazone (species election) in the reply filed on June 18, 2007 is acknowledged.

2. Claims 98-102, 104, 108, 112, 116, 122, 123, 138, 242-244, 246-250, 291- 292, 294-298, 339-340, 342-346, 387 and 388-394 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on June 18, 2007.

Notice of Non-Responsive Amendment mailed April 4, 2008

3. The Notice of Non-Responsive Amendment mailed on April 4, 2008 has been vacated.

Applicant's Response Dated December 31, 2007

4. Claims 95-102, 104, 108, 112, 116, 120-132, 138, 147, 151 and 168-397 are pending. Claims 98-102, 104, 108, 112, 116, 122, 123, 138, 242-244, 246-250, 291-292, 294-298, 339-340, 342-346, 387 and 388-394 are drawn to a nonelected species. An action on the merits of claims 95-97, 120-121, 124-132, 147, 151, 168-241, 245-249, 257-290, 293, 299-338, 341, 347-386, 389, and 395-397 is contained herein.

5. Applicant's arguments with respect to claims 142, 146, 152-155 and 164-167 under 35 U.S.C. 112, first paragraph, have been considered but are moot in view of the new ground(s) of rejection.

6. The rejection of claims 103, 120-121, 124, 148-149, 153-155, 157-158, 161-162 and 165-166 under 35 U.S.C. 112, second paragraph, as being indefinite, has been rendered moot in view of applicant's amendment dated December 31, 2007.

7. Applicant's arguments, see page 156, filed December 31, 2007, with respect to the rejection of claims 95-97, 103, 120-121, 124, 127-132, 142-146, 148-149, 153-155, 157-159, 161-163 and 165-167 under 35 U.S.C. 103(a) as being unpatentable over Sahoo et al. US 6,008,237 (Sahoo) in combination with Dang et al. US 6,284,748 (Dang) have been fully considered and are persuasive. The rejection of claims 95-97, 103, 120-121, 124, 127-132, 142-146, 148-149, 153-155, 157-159, 161-163 and 165-167 under 35 U.S.C. 103(a) has been withdrawn.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 95-97, 120-121, 124-132, 168-241, 245-249, 251-290, 293, 299-338, 341, 347-386, 389, and 395-397 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a mammal having diabetes comprising the administration of a pharmaceutically effective amount of an

insulin sensitizer agent and a pharmaceutically effective amount of an FBPase inhibitor or prodrug or salt thereof, wherein said insulin sensitizer agent is troglitazone or rosiglitazone and wherein said FBPase inhibitor is Compound A, B, C, D, E, F, G, H, I, J or K, does not reasonably provide enablement for treating a mammal having diabetes comprising the administration of a pharmaceutically effective with any compound of formula I or IA in combination with any insulin sensitizer agent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include, but are not limited to:

1. the breadth of the claims;
2. the nature of the invention;
3. the state of the prior art;
4. the level of one of ordinary skill in the art;
5. the level of predictability in the art;
6. the amount of direction provided by the inventor;
7. the existence of working examples; and
8. the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Claims 95-97, 120-121, 124-132, 147, 151, 168-241, 245-249, 251-290, 293, 299-338, 341, 347-386, 389, and 395-397 are drawn to method of treating a mammal having diabetes comprising the administration of a pharmaceutically effective amount of an insulin sensitizer agent and a pharmaceutically effective amount of an FBPase inhibitor or prodrug or salt thereof.

Undue experimentation is required to determine which compounds would be useful as an insulin sensitizer agent and/or FBPase inhibitor for which the instant invention is applicable and to determine which of these combinations would be useful in treating diabetes in a mammal. There has not been provided adequate guidance in the written description for accomplishing such, as only Compounds A-K (FBPase inhibitor) in combination with troglitazone or rosiglitazone (insulin sensitizer agent) were assessed, out of the numerous insulin sensitizer agents known in the art, not to mention the near infinite number of compounds and classes of compounds embraced by the instantly claimed formulae I and IA. While it is noted that an assay has been described for identifying other FBPase inhibitors, without guidance as to what molecules would likely effect FBPase activity, undue trial and error experimentation would be required to screen through the myriad of different chemical molecules embraced by formulae I and IA to determine those with the desired FBPase inhibiting activity and that would function in the claimed method of treating diabetes. There is nothing inherently wrong with defining some part of an invention in functional terms; however, a functional limitation must be evaluated and considered, just like any other limitation of the claim, for what it fairly conveys to a person of ordinary skill in the pertinent art in the context in which it is

used. Functional descriptions of chemical compounds/compositions must be coupled with a known or disclosed correlation between function and structure. It is also noted that there is a great deal of unpredictability in the art.

The compounds of formulae I and IA do not share a common, substantial chemical core. Further, Compounds A-K do not share a common, substantial chemical core. There is no discernable pattern as to which compounds of formula I or IA would inhibit FBPase activity. The art at the time the invention was made fails to establish predictability with regard to the properties of the FBPase inhibitors and insulin sensitizer agents needed to perform the methods as instantly claimed. It is noted that while there are some working examples using certain compounds of formula I or IA (Compounds A-K) in combination with troglitazone or rosiglitazone, it is not seen as sufficient to support the breath of the claims. The instant specification is not seen to provide adequate guidance which would allow the skilled artisan to extrapolate from the disclosure and examples provided to enable the use of any other compounds of formula I or IA or other insulin sensitizer agents. It is noted that Law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use it for themselves. See *In re Gardner* et al. 166 USPQ 138 (CCPA 1970).

Conclusion

10. Claims 95-102, 104, 108, 112, 116, 120-132, 138, 147, 151 and 168-397 are pending. Claims 98-102, 104, 108, 112, 116, 122, 123, 138, 242-244, 250, 291- 292,

294-298, 339-340, 342-346, 387 and 388-394 are drawn to a nonelected species. Claims 95-97, 120-121, 124-132, 147, 151, 168-241, 245-249, 251-290, 293, 299-338, 341, 347-386, 389, and 395-397 are rejected. Claims 147 and 151 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. No claims are allowed.

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on Monday - Friday 10 am to 3 pm (Maxi Flex).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Dr. Patrick T. Lewis/
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